

## REMARKS

Applicants respectfully request the Examiner to reconsider the rejections in view of the following remarks.

### I. Amendments to the Claims

Upon entry of the foregoing amendment, claims 1-8 and 15-24 are pending in the Application. Claims 7 and 18 are amended. Claims 9-14 are canceled without prejudice. New claims 23 and 24 are added.

Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter. Support for the amendments to the claims can be found throughout the specification (considered as a whole) and in the claims as originally filed. In particular, support for the amendment to Claim 7 can be found, *inter alia*, in the specification at page 10, line 30 to page 11, line 3. Support for the amendment to Claim 18 can be found, *inter alia*, in the specification at page 10, lines 1-8. Support for new claim 23 can be found, *inter alia*, in the specification at page 11, lines 13-23, and in claims 9-14 as originally filed. Support for new claim 24 can be found, *inter alia*, in the specification at page 6, lines 2-6.

Based on the instant amendment and remarks, Applicants respectfully request that the Examiner withdraw the outstanding rejections.

### II. Claim Objections

The Office Action stated that claims 15-20 and 22 are objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claims 9-14 and 9, respectively. *See* Office Action, p. 2. Applicants respectfully traverse these objections.

The Office Action asserts, “The only difference in these claims is the use of the term ‘cell-free system’ in claims 9-14 and ‘cell-free extract’ in claims 15-20. It is unclear however these two phrases differ and thus the claims appear to be duplicates.” *See id.* Applicants respectfully submit that a cell-free extract is a component of a cell-free system, as described in the specification on page 11, lines 13-23. Accordingly, and in the interest of furthering prosecution, Applicants have canceled claims 9-14 and added new claim 23, which recites a cell-free system comprising a cell-free extract.

For at least the foregoing reasons, Applicants respectfully request that the objections to

claims 15-20 and 22 under 37 C.F.R. § 1.75 be reconsidered and withdrawn.

### **III. Rejection Under 35 U.S.C. § 112, ¶ 2**

The Office Action stated that claims 7, 12, and 18 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. *See* Office Action, pp. 2-3. Applicants respectfully traverse this rejection.

The Office Action asserts that claim 7 “is vague in the recitation of ‘adapting ATP sulfurylase concentration according to the experimental conditions and the biological macromolecules to be synthesized’ as it is unclear what acts this encompasses.” *See id.* Applicants respectfully disagree since the Examiner was able to ascertain that the recitation was “synonymous with adjusting the ATP sulfurylase concentration to optimize the amount of protein synthesized.” *See id.* at p. 3. However, in the interest of furthering prosecution, Applicants have amended claim 7 accordingly.

The Office Action also asserted that claims 12 and 18 “are indefinite in the recitation of ‘derived from’ as it is unclear if this is synonymous with ‘isolated from’ or if it includes other things. Furthermore it is unclear how a protein is ‘derived from’ a vector as vectors do not comprise proteins.” *See id.* Applicants respectfully submit that one of ordinary skill in the art would understand the meaning of the term “derived from” in the context of claims 12 and 18. However, as mentioned in Section II above, claim 12 is canceled. In addition, claim 18 is amended to replace “derived from” with “expressed by” to clarify any ambiguity and thus, furthering prosecution.

For at least the foregoing reasons, Applicants respectfully request that the rejection of claims 7, 12, and 18 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

### **IV. Rejection Under 35 U.S.C. § 103(a)**

The Office Action stated that claims 1-22 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over International Application Publication No. WO 98/22615, in the name of Blakesley (“Blakesley”) in view of International Application Publication No. WO 00/55353, in the name of Swartz et al. (“Swartz”). *See* Office Action, pp. 4-5. Applicants respectfully traverse this rejection.

The examiner bears the initial burden of establishing a *prima facie* case of obviousness.

If the examiner does not satisfy his/her burden, then the applicant is not obligated to submit evidence of nonobviousness. *See M.P.E.P. § 2142 at 2100-125 (8th ed., rev. no. 5).*

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

*Id.*

The Office Action asserts, “As the [*in vitro* transcription/translation (“ITT”)] systems of Swartz et al. clearly require nucleic acid synthesis, it would have been obvious to one of ordinary skill in the art to employ the method of enhancing nucleic acid synthesis described by Blakesley et al. [sic] as Blakesley et al. [sic] clearly suggest that the disclosed methods would be useful for any system in which improvement of synthesis of nucleic acids by a polymerase is desired.” *See* Office Action, p. 5. Applicants respectfully disagree.

First, one of ordinary skill in the art would not be motivated to combine Blakesley with Swartz. The Office Action admits that Blakesley describes methods for preventing inhibition of nucleic acid synthesis by adding ATP sulfate adenyltransferase (*i.e.*, ATP sulfurylase). *See* Office Action, p. 4. Blakesley describes nucleic acid synthesis that is inhibited by pyrophosphorolysis, which is then prevented by adding enzymes to remove pyrophosphate. *See* Blakesley, Abstract.

Swartz, on the other hand, describes *in vitro* protein synthesis using novel ATP regeneration systems in which an energy homeostatic system is accomplished by the addition of a secondary energy source that indirectly provides high energy phosphate bonds without the release of free phosphate. *See* Swartz, p. 5, ll. 2-4 and p. 6, ll. 3-5. Therefore, the net accumulation of free phosphate, which can have an inhibitory effect on synthetic reactions, is prevented. *See id.* at p.6, ll. 10-11.

One of ordinary skill in the art would not be motivated to combine or modify the protein synthesis method of Swartz with the nucleic acid synthesis method of Blakesley because they are two different processes. In addition, because Swartz’s method prevents the accumulation of free phosphate, there would be no reason to combine the method of Blakesley, which provides a

method for eliminating inorganic pyrophosphate from the reaction mixture by adding ATP sulfurylase, with Swartz's method or to modify Swartz's method by adding ATP sulfurylase. Moreover, Swartz is concerned with improved protein synthesis, not improved nucleic acid synthesis. Therefore, contrary to the Office Action's assertion, Swartz would not employ the nucleic acid synthesis method described in Blakesley because Swartz uses optimized concentrations of commercial DNA or independently prepared DNA for protein synthesis.

Second, even if one of ordinary skill in the art were to combine or modify the method of Swartz with the method of Blakesley, he/she would not have a reasonable expectation of successfully achieving the claimed invention. The present invention uses the addition of ATP sulfurylase to enhance protein synthesis by regenerating ATP from the accumulated free inorganic phosphate in an *in vitro* transcription-translation cell-free system. However, Blakesley discloses the use of ATP sulfurylase to prevent inhibition of nucleic acid synthesis by pyrophosphorolysis, and Swartz eliminates the accumulation of phosphate altogether. One could not reasonably expect that a combination of two different processes (nucleic acid synthesis v. protein synthesis) with two different goals (preventing pyrophosphorolysis v. eliminating the accumulation of phosphate) would successfully achieve an enhanced method for protein synthesis with a completely different goal of generating ATP by using ATP sulfurylase to bind accumulated phosphate.

For at least the foregoing reasons, Applicants respectfully request that the rejection of claims 1-22 under 35 U.S.C. § 1.3(b) be reconsidered and withdrawn.

### CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed or rendered moot. Applicants, therefore, respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

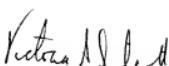
The Examiner is respectfully requested to contact the undersigned by telephone at the below listed telephone number, in order to expedite resolution of any issues and to expedite passage of the present application to issue, if any comments, questions, or suggestions arise in connection with the present application.

Respectfully submitted,

HUNTON & WILLIAMS LLP

Date: August 2, 2007

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